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Nancy's Next Campaign

The former First Lady's passion for Stem-Cell Research has fueled a political battle. Where does the science stand?

By **Claudia Kalb and Debra Rosenberg**
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June 21 issue - One spring afternoon in 2002, eight long years into her husband's descent into Alzheimer's, Nancy Reagan went to her friend Doug Wick's home in Los Angeles for a Hollywood-style tutorial on stem cells. Along with Wick and his wife, Lucy, both producers, the cast included moviemakers Jerry and Janet Zucker, actor Warren Beatty and Dr. Richard Klausner, now head of global health at the Bill & Melinda Gates Foundation. Nancy Reagan already knew a bit about stem cells—a year earlier, she'd written a letter to President Bush asking him to support embryonic research—but she was eager to delve deeper. Together the group discussed the ethics, the politics and the science. "She asked a lot of questions about what [stem cells] were, where they came from," says Klausner. Nancy

knew it was too late to rescue her husband, but she "had a higher purpose," says Wick. "She feels the greatest legacy her family could ever have is to spare other families from going through what they have."

After the meeting, Nancy began making her views known behind the scenes, respectfully but forcefully—calling politicians, conversing with scientists, buttonholing lawmakers at the rare Washington dinner she allowed herself. Then last month Reagan decided to go public at a Juvenile Diabetes Research Foundation gala, and she asked others to join in her quest. "Science has presented us with a hope called stem-cell research, which may provide our scientists with answers that have so long been beyond our grasp," she said. "I just don't see how we can turn our backs on this—there are just so many diseases that can be cured, or at least helped. We have lost so much time already, and I just really can't bear to lose any more."

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Nancy Reagan's bold challenge to her own Republican Party and to Bush's 2001 policy on embryonic research was a pivotal moment for stem-cell advocates. For months they had been rallying across the country; with Nancy's support, and now with her husband's death and heroic farewell, they have found fresh momentum. Last week in Washington, 58 senators, including John Kerry, sent a letter to the White House, urging Bush to relax his restrictions on embryonic-stem-cell research. In a radio address to the nation over the weekend, Kerry reaffirmed his commitment to overturning Bush's policy if elected. On the West Coast, meanwhile, Californians for Stem Cell Research and Cures celebrated the collection of 1 million signatures authorizing a \$3 billion stem-cell-research initiative to be put to the vote in November. In Boston 1,400 scientists gathered to discuss both embryonic and adult stem cells at a meeting of the International Society for Stem Cell Research (ISSCR), where the embryonic-stem-cell advocate and Republican senator Arlen Specter encouraged them to stand up for science. "We need more political activism," he told the group. "The marvels of modern science should obviously not be shackled." Newspapers ran editorials calling on Bush to honor Ronald Reagan's legacy by revising his stem-cell policy—"George should do it for the Gipper," said one—and a New York congressman introduced the Ronald Reagan Memorial Stem Cell Research Act of 2004.

All of this infuriated embryonic opponents: one senior Republican aide said naming stem-cell legislation after the president, who was ardently opposed to abortion, was "unbelievably shameless." But out of respect for Reagan, the adversaries mostly held their fire. Bush stayed mum, but privately officials said he would not budge on his opposition to destroying human embryos for the sake of science. "No dramatic advance, no scientific development will change the ethical principle" underlying Bush's position, a senior administration official told NEWSWEEK last week. Laura Bush, whose father died of Alzheimer's, made the media rounds instead, gently reiterating the administration's position on stem-cell research without attacking Nancy head-on. "We have to be really careful between what we want to do for science and what we should do ethical-ly," she told CBS. When she was asked if she would endorse additional stem-cell research, the answer was clear: "No."

What is it about embryonic stem cells? How can these microscopic flecks galvanize scientists and celebrities and, at the same time, pit First Ladies against each other and turn political allies into formidable foes? Under the microscope, embryonic stem cells look like luminous stars in a black-and-white galaxy. Just days old, they have the extraordinary capacity to become any one of the more than 200 cell types that make up the human body—from heart to brain to muscle. Researchers believe they may hold the key to curing or at least revolutionizing our understanding of deadly diseases like Parkinson's, diabetes and Alzheimer's. But no matter how mysterious or magical their powers, the cells are culled from human embryos, and to those who consider the fusion of sperm and egg sacred life—whether it takes place in a womb or a lab dish—they are morally off-limits for research.

In an effort to placate both scientists and pro-life constituents, Bush announced a compromise policy on Aug. 9, 2001: federal funds, which underwrite the vast majority of scientific research in this country, could be used to study embryonic stem cells, but only those that had already been isolated in the lab and grown into stem-cell "lines." Almost immediately scientists began complaining that the restrictions would inhibit their work. The administration said as many as 78 lines existed, but that number turned out to be inflated; as of last week only 19 were available. (Other lines exist but can be worked on only with private money.) Scientists say the lines are often difficult to obtain and of questionable quality. "It's like forcing us to work with Microsoft version 1.0 when the rest of the world is already working with 6.2," says biologist David Anderson of Caltech. Without better access to embryonic stem cells, U.S. scientists worry that they're in danger of becoming bystanders to medical innovation.

Political support for embryonic-stem-cell research—galvanized by testimony from scientists and the heart-wrenching stories of sick Americans pleading for cures—has come from surprising quarters. Rep. Duke Cunningham, a pro-life Republican from California, says he

is haunted by a child who told him, "Congressman, you're the only person who can save my life." He signed on after a scientist explained that IVF clinics house thousands of frozen embryos, from which stem cells are derived, and that many are destined to be discarded. "My own personal belief is that I'm actually saving life from something that is not going to be life," he says. Sen. Orrin Hatch, a Mormon from Utah who is staunchly pro-life, is an ardent supporter, too. In early 2003 he, Specter and Democratic senators Ted Kennedy, Dianne Feinstein and Tom Harkin introduced a bill that, with strict regulations, would allow so-called therapeutic cloning to create new embryos from which more stem cells could be harvested. Along the way, Nancy Reagan spoke with both Republican senators and sent Hatch a note backing the legislation. "She's a conservative woman, very much like her husband," says Hatch. "The fact that she's been willing to speak out on this has been very helpful."

Today 4.5 million Americans suffer from Alzheimer's, a number that is expected to spike to 16 million by 2050. Scientists and drug companies are rushing to improve diagnosis and treatment with brain imaging, medications and even an experimental vaccine. But as Nancy Reagan knows better than anyone, available therapies address symptoms only and are unable to halt the ravaging disease, let alone cure it altogether. That's where her passion for stem cells comes in. Already researchers have been able to coax embryonic stem cells into neurons that produce dopamine, the culprits in Parkinson's. Might scientists also find a way to transform them into the neurons damaged by Alzheimer's, then transplant the healthy new cells into a patient's brain? Nobody knows. The reality is that Alzheimer's is so complicated that even miraculous stem cells might not cure it. Harvard neurologist Rudy Tanzi likens the Alzheimer's brain to a defunct stereo. You can't "throw in a bunch of capacitors and transistors and expect to hear music," he says. "You have to rewire the system."

Maria Shriver, whose father has Alzheimer's and who has forged an alliance with Nancy Reagan on stem cells, believes the research could help uncover the illness's genetic link: "It will help millions of children of people with this disease." At the University of California, San Diego, Dr. Larry Goldstein is using embryonic stem cells to develop human brain cells that carry Alzheimer's mutations. Rather than analyze the disease in its later stages, he wants to watch it develop from the beginning, with the hope of creating drugs to stop its progress early on. Ultimately, scientists believe embryonic stem cells will be able to shine a light on the fundamentals of human biology. "It's not just that stem cells will magically cure disease, they can help us understand how life emerges," says stem-cell researcher Ron McKay of the National Institutes of Health. "This is the future of medicine."

When stem cells are involved, however, the future of medicine is never just about medicine—it's about politics, too. Scientific studies become ammunition to support a particular viewpoint; medical data, no matter how nuanced, get spun with political finesse. Now adult stem cells, derived from mature human beings rather than days-old embryos, have become pawns in the debate. The administration and right-to-life groups praise their potential, offering them up as equally powerful as embryonic stem cells, if not more so. Several years ago, research backed those claims, suggesting that adult stem cells were indeed far more "plastic" than anyone had dreamed. But now some scientists are challenging those findings. "People are starting to realize that the science of plasticity is not all there," says Dr. Leonard Zon, ISSCR president.

Unlike embryonic stem cells, adult stem cells are prewired to become a particular kind of tissue—skin, intestine or blood, for example. Like theatrical understudies, they stand in the wings, rushing in only when cells need replenishment after injury or disease. Scientists know the most about the adult stem cells of the blood, which are given in bone-marrow transplants to patients with cancer or blood diseases. That success prompted researchers to wonder: could adult blood stem cells have the same acrobatic ability as embryonic stem cells? Dr. Markus Grompe, of Oregon Health & Science University, initially thought yes. In 2000 he reported that adult blood stem cells were able to turn into liver cells in mice. But two years later Grompe reassessed his data and came to a different conclusion: the blood cells had fused with existing liver cells—more a case of biological identity theft than transformation.

New studies are now questioning earlier work on heart disease, too. In 2001, news that adult bone-marrow stem cells had become cardiac muscle in mice spurred great hope, even leading to clinical trials in humans. Dr. Piero Anversa, of New York Medical College, worked on the original research and stands by it "1,000 percent." But in April two groups reported that they could not reproduce the finding, a critical step in the validation of science. "Our paper says it doesn't work," says Stanford University's Dr. Irv Weissman.

The holy grail for many scientists is a cure for type 1 diabetes, the disease that plagues Doug Wick's daughter and helped spark Nancy Reagan's interest in stem cells. For years researchers have searched for adult stem cells in the pancreas, hoping such cells could make themselves into insulin-producing beta cells, which diabetics lack. But last month Harvard biologist Doug Melton dashed the hopes of many when he reported that he could find no adult stem cells in the pancreas at all. His conclusion: "If you want to make more beta cells, the place to look is embryonic stem cells."

Stem-cell science is still early in development—too early to make absolute statements about what works and what doesn't. Even the most passionate supporters of embryonic research believe the study of adult stem cells should proceed with equal vigor. Embryonic stem cells are the gold standard in versatility, but adult stem cells still hold promise, especially for repair within their own tissue family.

